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The claims have been revised to define the invention with additional clarity. The language suggested by the Examiner in paragraph (3) of the Action has been adapted, thereby mooting the Examiner's objection to claims 2-11.

Claims 2-11 stand rejected under 35 USC 112, second paragraph, as allegedly being indefinite. Withdrawal of the rejection is submitted to be in order for the reasons that follow.

Claim 2 has been amended to include the additional steps of (i) determining interaction in the absence of test compound and (ii) comparing interaction in the presence relative to the absence of test compound. Corresponding amendments have also been made to claims 4 and 5 as appropriate. The full form of the term 'CBP' has been included at its first occurrence in claim 2. Further, the generic term 'Importin α activity' has been replaced by the list of specific Importin α activities that were originally set out in now cancelled claim 3.

The term 'and/or' has been replaced by conventional Markush wording in claims 5 and 8.

The Examiner considers the phrase 'determining interaction between the first and second substances' in claim 4 to be indefinite because it is allegedly unclear

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how the interaction between these substances might be determined. Applicant respectfully disagrees.

The present invention is directed towards methods of screening for compounds that inhibit Importin α activity via the Importin α /CBP interaction. The invention is not specifically concerned with methods of measuring protein interaction. That said, many suitable techniques were available in the art to determine the interaction between two proteins. Examples of suitable techniques are discussed on page 27, line 15, to page 28, line 5, and page 31, line 16, to page 35, line 9, of the specification.

A person of ordinary skill in the art would be aware of numerous ways in which protein interactions can be determined, in the context of a screening method. The specific technique adopted is not important, as long as it enables the interaction between the substances to be determined. The determination of interaction represents a clear and definite method step which a skilled artisan would have had no difficulty in performing using one of a range of different techniques and approaches, all of which were well known in the art.

The Examiner contends that claim 5 is indefinite because it does not indicate how the effect of an agent on

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the ability of Importin α to bind Importin β , translocate into the nucleus or import a cargo protein is determined.

The wording to the claim 5 has been amended to emphasize that the effect of an agent on the ability of Importin α to bind Importin β , translocate into the nucleus or import a cargo protein is determined through the determination of the effect of the agent on CBP acetyltransferase activity. The recognition that CBP acetyltransferase activity modulates the activity of Importin α is part of the inventive contribution made by Applicant.

A skilled person would be readily able to determine acetyltransferase activity using standard techniques, such as those described on page 37, line 10, to page 40, line 10, of the specification, in order to identify an agent which would affect the activity of Importin α by modulating its acetylation by CBP. Furthermore, the skilled person would also be able to confirm the effect of such an agent by measuring Importin α activity directly, using techniques which are also readily available in the art, for example, as described on page 30, line 18, to page 31, line 14, of the specification.

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The wording of claim 9 has been amended to emphasize the meaning of the terms 'a region Importin α ' and 'a said region'.

For the reasons set out above, it is respectfully submitted that the expression 'determining interaction between said substance and said test compound' has a definite meaning and a skilled person would have a clear understanding of what this method step involves and how to carry it out using any one of a number of techniques readily available in the art.

Claim 10 has been amended to exclude non-elected subject matter and to include the subject matter of now cancelled claim 11.

In view of the above, it is submitted that claims meet the requirements of 35 USC 112, second paragraph. Reconsideration of the rejection is, therefore, requested.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached pages are captioned "Version With Markings To Show Changes Made."

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This application is submitted to be in condition for allowance and a Notice to that effect is requested.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

2. (Amended) An assay method for identifying an agent which affects one or more Importin α [activity] activities selected from the group consisting of (i) binding Importin β , (ii) translocating into the nucleus, and (iii) importing a cargo protein; the method including:
- (d) bringing into contact Importin α and a test compound [and];
- (e) determining said one or more Importin α [activity] activities in the presence and absence of a CBP ('CREB binding protein') polypeptide which acetylates Importin α , thereby determining the effect of said polypeptide on said one or more activities, and;
- (f) comparing said effect in the presence of test compound with said effect in absence of test compound, a difference in said effect in the presence relative to the absence of test compound being indicative that said test compound is an agent which affects said one or more Importin α activities.

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4. (Amended) An assay method for identifying an agent which modulates interaction between CBP and Importin α , the method including:

(a) bringing into contact a first substance including a CBP polypeptide or peptide, a second substance including an Importin α polypeptide or peptide, and a test compound under conditions in which, in the absence of the test compound being an inhibitor, the first and second substances interact; [and]

(c) determining interaction between the first and second substances, and;

(c) comparing said interaction in the presence of test compound with said interaction the absence of test compound,

a difference said interaction in the presence relative to the absence of test compound being indicative that said test compound is an agent which modulates interaction between CBP and Importin α .

5. (Amended) An assay method for identifying an agent which affects [ability] one or more activities of Importin α [to] selected from the group consisting of (i) [bind] binding Importin β , (ii) [translocate] translocating

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into the nucleus, [and/or] and (iii) [import] importing a cargo protein, the method comprising:

(c) bringing into contact CBP and a test compound, [and]

(d) determining CBP acetyltransferase activity in the presence and absence of the test compound; and

(c) comparing said CBP acetyltransferase activity in the presence of test compound with said activity in the absence of test compound,

[wherein] a decrease in CBP acetyltransferase activity in the presence relative to the absence of the compound being indicative that the [a] test compound [which inhibits CBP acetyltransferase activity is identified as a candidate said agent] is an agent which affects said one or more activities of Importin α .

8. (Twice Amended) A method according to claim 5 wherein a test compound which inhibits CBP acetyltransferase activity is further tested for ability to affect [ability of] an activity of Importin α [to] selected from the group consisting of (i) [bind] binding Importin β , (ii) [translocate] translocating into the nucleus, [and/or] and (iii) [import] importing a cargo protein.

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9. (Amended) An assay method for identifying an agent which interacts with a region of CBP or a region of Importin α , which region of CBP interacts with Importin α and which region of Importin α interacts with CBP, a said agent which interacts with said region of CBP or said region of Importin α being a candidate modulator of interaction between CBP and Importin α , the method including:

(c) bringing into contact a substance which includes a CBP peptide which interacts with Importin α , or which includes an Importin α peptide which interacts with CBP, and a test compound; and

(d) determining interaction between said substance and the test compound,

the presence of interaction between said substance and the test compound being indicative that the test compound is a said agent.

10. (Twice Amended) A method according to claim 1, claim 4, claim 5 or claim 9 further comprising formulating a said agent [or, optionally where said agent is peptidyl, nucleic acid encoding said agent,] into a composition comprising [at least one additional component] a pharmaceutically acceptable excipient.